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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
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EXAMINER
LOEB, BRONWEN

ART UNIT	PAPER NUMBER
1636	12

DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/516,310	LIN ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-26 and 33-38* is/are pending in the application.

4a) Of the above claim(s) *16-26 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-15 and 34-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 March 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This action is in response to the amendment filed 9 December 2002 in which claims 6, 8, 16 and 26 were amended and new claims 34-38 were provided.

Claims 6-26 and 33-38 are pending.

Election/Restrictions

1. Claims 16-26 and 33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

2. It is noted that Applicant has amended non-elected claims 16 and 26. While these amendments have been entered, the claims remain withdrawn from consideration as they are drawn to a non-elected invention. It is further noted that these amendments have not been examined in any way.

3. New claims 34-38 are dependent on claim 6 and are examined herein as part of the elected invention.

Drawings

4. Applicant is required to submit a proposed drawing correction in reply to this Office action with respect to the Draftsperson's Review of the Patent Drawings, Form 948, attached to the action mailed 3 June 2002. However, formal correction of the noted defects may be deferred until after the examiner has considered the proposed

drawing corrections. Failure to timely submit the proposed drawing correction will result in the abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

5. Claim 6 is objected to because of the following informalities: The Markush group which is recited starting on line 5 and continuing through line 12, has 5 members: a protein or a portion of a protein, a portion of a nucleic acid, a carbohydrate, a lipid and a glycolipid. The claim formatting should reflect this by adding a (iv) before lipid and an (v) before glycolipid. Appropriate correction is required.

Response to Amendment

6. The rejection of claim 8 under 35 USC §112, first paragraph for insufficient written description has been withdrawn in view of Applicant's amendment.

The rejection of claims 9 and 12 under under 35 USC §112, first paragraph for insufficient written description has been withdrawn.

7. The declaration under 37 CFR 1.132 filed 9 December 2002 is insufficient to overcome the rejection of claims 6-15 based upon insufficiency of disclosure under 35 USC §112, first paragraph as set forth in the last Office action because: it provides a review of literature published after the effective filing date of the instant invention and offers no objective data to support enablement commensurate with the scope of the

claims. On the contrary, the declaration appears to be little more than the opinion of Applicant's representative and as such, holds little or no weight.

8. Claims 6-15, and new claims 34-38, stand rejected under 35 USC §112, first paragraph for lack of enablement for reasons of record and as further discussed below.

Claims 6-8, 10, 11, 13-15, and new claims 34-38, are rejected under 35 USC §112, first paragraph for insufficient written description.

9. New grounds of rejection, necessitated by Applicant's amendment, are set forth below.

Response to Arguments

10. With respect to the rejection of claims 6-15 under 35 USC §112, first paragraph for lack of enablement, Applicant's arguments have been fully considered but are deemed not persuasive.

First it is noted that Applicant repeatedly makes arguments with respect to a utility rejection under 35 USC §101 (see for instance p. 6, first and third paragraphs and p. 7, line 2 "lack of credible utility"). These arguments are not germane to the outstanding rejection which is one under 35 USC §112, first paragraph. See MPEP 2164.07. Thus the issue at hand is not the lack of a credible use, as Applicant repeatedly and mistakenly argues, it is the lack of enabled use.

Applicant describes the claimed invention as "a method of treating a cell" (p. 6, third paragraph). This statement does fully reflect the pending claims which are drawn to "a cell in a subject". Furthermore, the specification clearly teaches the methods for use in treatment (p. 1, lines 19-20 and 24, p. 3, lines 9-17 and p. 19, line 10-p. 20, line

7). While it is true that the claims are not limited to gene therapy (which is the delivery of a nucleic acid for therapeutic purposes), the methods clearly encompass gene therapy and are clearly for treatment in a subject.

Applicant argues that the art relied upon by the Office does not support a prima facie showing of lack of credible utility. As discussed above, the pending rejection is a lack of enabled use not a lack of credible utility. The references cited with part of a complete and proper analysis of the Forman factors and they demonstrate what experts in the field of gene therapy consider the on-going obstacles with achieving successful gene therapy.

Under the section entitled "Guidance" Applicant sets forth general guidelines derived from various cases regarding 35 USC §112, first paragraph and points to the Sundsmo declaration filed 9 December 2002. As discussed above, the declaration does not overcome the pending rejection. With regard to the general guidelines Applicant sets forth, Applicant is reminded that enablement must be commensurate in scope with the claims. MPEP 2164.08. Thus broad claims require a commensurate broad scope of enablement. Furthermore, the amount of guidance needed to enable an invention is inversely related to the amount of knowledge in the prior art as well as predictability. See MPEP 2164.03. In unpredictable fields, such as gene therapy, the amount of guidance is very high to enable claims encompassing it.

Applicant summarizes four aspects, mixing, coupling, peptide synthesis and clinical delivery, dosing and formulation of protein and peptide-based active pharmaceutical ingredients and asserts that undue experimentation is not required to

use the claimed invention. With regard to mixing, coupling and peptide synthesis, these aspects are not considered a problem with regard to enablement. With regard to clinical delivery, however, the assertion that the method is enabled for methods using protein and peptide-based complexes is not persuasive. The claimed methods use a complex comprising an "importation competent signal peptide". The specification demonstrates for one importation competent signal peptide importation into NIH 3T3 cells and discloses that any cell type can be used. Since this importation into any cell type is presumably mediated by the importation competent signal peptide, targeting the complex to the desired cells to achieve a therapeutic effect and avoiding systemic importation into all cells is critical. Neither the prior art nor the instant specification provide sufficient guidance to one of skill in the art answer such questions. With regard to the delivery of nucleic acids, Applicant has notably failed to address the expert-acknowledged obstacles: delivery efficiency and sufficiency of expression.

Applicant reproduces large portions of the specification on pp. 11-14 and 17 of their argument. Applicant is reminded that the specification was considered in setting forth the original rejection. Reproducing these sections is not persuasive.

Applicant summarizes a series of post-filing references to demonstrate the proven "utility of the claimed methods and exciting promising future therapeutics currently under development" (p. 15). Applicant is again reminded that the claimed methods must be enabled by the specification as filed; the post-filing publications, none of which appears to support enablement commensurate with the scope of the claims, do not overcome the rejection.

It is noted that with regard to new claim 34, the specification fails to teach any specific peptide therapeutic drug agents for the various diseases recited in claim 34. This failure requires one of skill in the art an additional large quantity of experimentation to determine for each of the diseases recited (which are themselves broad classes of diseases and not a specific disease) what peptide would serve as a therapeutic for that disease.

In summary, Applicant's arguments are not persuasive individually or when considered as a whole. The rejection is therefore maintained.

11. With respect to the rejection of claims 6-15 under 35 USC §112, first paragraph for insufficient written description, Applicant's arguments have been fully considered but are deemed not persuasive.

Applicant argues that the skill in the art is high and that the specification teaches experimental methods by which competent importation signal peptides can be identified. Experimental methods for how to identify these signal peptides, while possibly germane to an enablement rejection, are not germane to a written description rejection (which is severable from enablement). With regard to written description, a specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully

set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Furthermore, as stated in MPEP 2163(I)(A) :

> A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

The specification teaches no structure-function correlation between specific amino acids and the importation function of the signal peptide. There is only the general teaching of being hydrophobic (p. 10, lines 24-30). It is clear that applicant did not have possession of the entire genus of importation signal peptides, but rather, only a method for how to identify one experimentally. The rejection is maintained.

New Grounds of Rejection

12. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 6-10 and 34-38 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended claim 6 is drawn to a method of importing a biologically active molecule into a cell in a subject wherein the biologically active molecule may be "a vaccine

polypeptide" and where the complex induces or inhibits a biological response including "a mitogenic response in the cell", "an inhibition of cell division in the cell" and "an inhibition of tyrosine phosphorylation in the cell". While the specification teaches several other biologically active molecules (p. 6) and other biological responses (p. 14-18), it does not teach or suggest any of the above specific recitations. These recitations are therefore deemed to be new matter and must be removed from the claims. This is a NEW MATTER rejection.

14. Claims 6-10 and 34-38 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed

invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

This rejection is based on the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 6 is drawn to a method of importing a biologically active molecule into a cell wherein the biologically active molecule is selected from the group which includes "an antigenic polypeptide" and "a portion of a protein". This is a genus claim in terms of any polypeptide that is antigenic, and any portion of any protein from the recited Markush group. The specification mentions a method using antigenic polypeptides (p. 14, line 30-p. 15, line 4 and p. 17, line 28-p. 18 line 3) and a general teaching about antigenic polypeptides (p. 7, lines 17-22). There is no discussion regarding "a portion of a protein". This disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all antigenic polypeptides and portions of a protein based on the teachings in the specification. There is no discussion of what amino acids or sequence motifs in a polypeptide render it antigenic. There is no structure-function relationship provided relating amino acid sequence to antigenicity. Likewise, there is no discussion of what portions of the recited proteins should be used that remain biologically active. There is no structure-function correlation provided for any single species of the various genuses recited (a growth factor polypeptide, an enzyme polypeptide, etc) that would indicate possession of those portions which are biologically active. There is no teaching

that there is a single structure-function relationship shared among all the genuses that relates sequence to biologically active portions. Therefore, the specification does not describe the claimed antigenic polypeptides or portions of proteins in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these antigenic polypeptides or protein portions at the time of filing the present application. Thus, the written description requirement has not been satisfied.

15. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 6-10 and 34-38 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is vague and indefinite in not employing proper Markush language. An example of proper Markush language is: "selected from the group consisting of: (first member), (second member)....and (final member)". Thus, the Markush group recited in (i) should have an "and" before the final recited member. Also the Markush group which is recited starting on line 5 of the claim lacks an "and" before the final element, which appears to be "a glycolipid".

Claim 6 is vague and indefinite in reciting "a vaccine polypeptide". This term is not defined in the specification nor it is a term of art.

Conclusion

Claims 6-15 and 34-38 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 11:00 AM to 7:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

February 14, 2003

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
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